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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,838	11/29/2001	Hans Hofland	P 23,643-A USA	6395

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EXAMINER

EPFS FORD, JANET L

ART UNIT	PAPER NUMBER
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1633

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/996,838	Applicant(s) HOFLAND ET AL.	
	Examiner Janet L. Epps-Ford	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,7,11,14,15 and 18-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,7,11,14,15 and 18-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 102

3. Claims 18-23, and 30 remain rejected under 35 U.S.C. 102(e) as being anticipated by Monahan et al., or unpatentable over Monahan et al. for the reasons of record set forth in the Final Office Action mailed 3-09-05.

Applicant's arguments filed 5-10-2007 have been fully considered, but they are not persuasive. Applicants have amended instant claim 18 to recite:

18. (Currently amended) A stable colloid ~~prepared by the process of Claim 1~~ comprising
an aqueous phase, and
a DNA complex which is suspended in said aqueous phase and which
has a neutral or net anionic surface potential and which consists essentially of
DNA attached ionically to and sequestered within lipids or polymers which are
chemically modified reaction products of: (A) a reagent selected from the group
consisting of citraconic anhydride and N-hydroxysuccinimide acetate; and (B)
cationic lipids or polymers.

Applicants argue that "[t]he novelty of the product claim is that the chemically modified lipid/polymers (by the claimed reagents) are ionically attached to the DNA. None of the prior art references discloses this structure." Moreover, Applicants argue that Monahan

et al. and Trubetskoy et al. teach adding a third layer of chemically modified polymers that are not "attached ionically to"

Contrary to Applicant's arguments, the instant rejection is over Monahan et al., not Trubetskoy et al. and Semple et al. Furthermore, absent evidence to the contrary, the transitional phrase "consisting essentially of," will be construed as equivalent to "comprising" (See, MPEP § 2111.03 [R-3]), since the specification as filed does not define what it regarded as constituting a material change in the basic and novel characteristics of the invention. Therefore, since claim 18 is drawn to a stable colloid, **comprising** a DNA complex, absent evidence to the contrary, the disclosure of Monahan et al. anticipates the instantly claimed invention, since they disclose a process for the formation of a stable colloid, wherein said process comprises that the addition of citraconic anhydride to the cationic polymer poly-L-lysine, and the formation of citraconylpoly-L-lysine, and the addition of this compound to a complex of DNA and poly-L-lysine, wherein the overall zeta potential of the formed particles of this reaction is negative (see col. 25, lines 27-65). Additionally, Monahan et al. teach the use of NHS ester to react with cationic polymers to form anionic polymers. Additionally, it is clear that the invention of Monahan et al. is specifically designed for modifying DNA-polymer complexes to comprise a negative zeta potential for the express purpose of delivering nucleic acid in cells (see abstract). Moreover, in regards to the "attached ionically to" limitation, there is no evidence that the amino groups of the poly-Lysine portion of the citraconylpoly-L-lysine polymers of Monahan et al. do not interact ionically with the DNA complexed within the complexes.

Claim Rejections - 35 USC § 103

4. The rejection of claims 1, 7, 11, 14-15, 18-23, and 24-32 under 35 USC § 103(a) as being unpatentable over Semple (US Patent No. 6,287,591 B1) taken with Trubetskoy (US 2003/0026841 A1) and Monahan et al. (6,379,966), is withdrawn in response to Applicant's arguments and amendment.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 7, 11, 14-15, 18-23, and 24-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (New Matter).

The instant claims 1, 7, 11, and 14-16 are drawn to a process for making a stable colloid for gene transfer comprising providing a colloid comprising an aqueous phase having suspended therein a DNA complex which consists essentially of DNA sequestered within cationic lipids or cationic polymers which has a cationic surface potential.

The specification as filed describes the claimed invention in the following manner:

[0009] The present invention provides methods and compositions for efficient DNA packaging in neutral or negatively charged colloids. In addition, this invention enables targeted delivery of DNA to a specific site in the body after systemic administration.

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[0010] Specifically, the present invention provides methods to reduce, eliminate or reverse the positive charge of particles obtained by complexation of a cationic component to the anionic DNA. The invention also contemplates the composition of the final colloid that enables targeted gene delivery. Preferred methods and compositions of the present invention provide advantages of efficient DNA packaging combined with particle stability in serum and targetability.

[0011] Therefore, according to one aspect of the present invention, a process for making **neutral or anionic complexes containing sequestered DNA** for gene transfer is provided, in which a stable colloid is formed wherein the aqueous phase has suspended therein a first DNA complex with a cationic surface potential containing a DNA sequence complexed with a cationic lipid or polymer, after which the surface potential of the first DNA complex is modified to form a stable colloid containing a second DNA complex with a neutral or net anionic surface potential.

In regards to the sequestering of DNA in a DNA/cationic lipid or polymer complex, the specification states:

[0035] *Stable particles containing active plasmid DNA can be produced using a self-assembling process where cationic lipids or cationic lipid/neutral lipid mixtures are attached to DNA by ionic interactions. The lipids are first put in aqueous suspension as micelles or liposomes. As these particles bind to DNA, a spontaneous rearrangement produces sections of lipids in bilayers sandwiching the DNA. **If enough lipid is used, all of the DNA becomes sequestered within the lipid structure and is unavailable to compounds in solution such as DNase.***

Moreover, original claim 1 recited:

1. A process for making **neutral or anionic complexes containing sequestered DNA** for gene transfer, comprising: forming a stable colloid comprising an aqueous phase having suspended therein a first DNA complex with a cationic surface potential comprising a DNA sequence complexed with a cationic lipid or polymer; and modifying the surface potential of said first DNA complex to form a stable colloid comprising a second DNA complex with a neutral or net anionic surface potential.

The specification as filed does not provide adequate support for the claimed process, wherein the process is initiated with DNA sequestered within the DNA/cationic lipid or liposome complex, and wherein said complex is subsequently treated with

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citraconic anhydride or N-hydroxysuccinimide ester. Based upon the teachings of the specification as filed, there is no information given in regards to how the original DNA/complex is formed, to provide clear support that sufficient lipid was used to form said complex such that the DNA is clearly sequestered within the complex. Moreover, it appears that the original objective of the claimed method was to form a stable colloid comprising neutral or anionic complexes comprising **sequestered DNA**.

Additionally, the specification as filed does not provide adequate support for stable colloids comprising an aqueous phase, and a DNA complex **consisting essentially of** DNA ionically attached to and **sequestered** within lipids or polymers, of undefined charge, which are chemically modified reaction products of citraconic anhydride and N-hydroxysuccinimide acetate and cationic lipids or polymers. The specification as filed does not describe what it regarded as constituting a material change in the basic and novel characteristics of the invention such that the ordinary skilled artisan would be able to ascertain what the term "consisting essentially of" encompasses as it relates to the instantly claimed stable colloids.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE